Nevertheless, all enzymes undergo conformational changes during their reaction cycles and an X-ray structure of a resting conformation alone describes only the starting point for the reaction. Time-resolved structural studies of protein reaction dynamics aim to elucidate the conformational changes occurring in proteins and thereby elucidate the chemical details of their reaction mechanism.

First I will describe structural results from time-resolved Laue diffraction studies of a photosynthetic reaction centre performed using synchrotron radiation. In this work we were able to observe conformational changes for a conserved tyrosine residue located near the reaction centre's special pair of chlorophyll molecules [1], which is photo-oxidised by light. Thereafter I will touch upon the implications of new approaches to time-resolved structural biology which can emerge from the revolutionary new approach of ultrafast nano-crystallography at X-ray free electron lasers [2]. I will describe both the potential benefits of single-shot time-resolved studies from micro-crystals at an X-ray free electron laser, and I will outline some of the challenges associated with time-resolved diffraction using larger crystals at these sources.

[1] A.B. Wöhri, et al. *Science* **2010,** *328,* 630-3; [2] H. Chapman, et al. *Nature* **2011,** *70,* 73-77.

Keywords: structural dynamics; jaue diffraction; X-ray free electron laser

MS.37.2

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3D imaging with coherent X-rays at nano-scale resolution and beyond

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Progress on coherent X-ray diffractive imaging technique has reached to its successful applications in unveiling three-dimensional structures of biological specimens at several tens of nanometer resolution and nano-structured materials at ten nanometers scale presently. Interest in achieving a few nm resolution is zealous. By overcoming difficulties accompanied by insufficient coherent X-ray flux and X-ray radiation damage to specimens, we expect 3D imaging of a biological cell or organelle at a few nm resolution to be realized in a near future. Further with X-ray free electron laser (XFEL), 3D imaging of small organelles and macro-protein complexes would be amenable at near atomic resolution. Together these will provide a complete picture of a cell with macromolecular details: a path to understand a biological system *ab initio*.

In this talk, I will introduce recent progress on 3D imaging of a yeast cell and others accomplished at SPring-8. Activities on imaging of biological specimens and nano-structures by using the prototype EUV FEL facility of SPring-8 Compact SASE Source will also be introduced.

[1] H. Jiang, C. Song, C-C. Chen, R. Xu, K. Raines, B. P. Fahmian, C-H. Lu, T.-K. Lee, A. Nakashima, J. Urano, F. Tamanoi, J. Miao, *Proc. Natl. Acad. Sci.* USA **2010**, *107*, 11234, [2] C. Song, H. Jiang, A.P. Mancuso, B. Amirbekian, L. Peng, R. Sun, S.S. Shah, Z.H. Zhoum T. Ishikawa, J. Miao, *Phys. Rev. Lett.,***2008,** *101*, 158101.

Keywords: coherent X-ray imaging, bio-imaging, free electron laser

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Structure and dynamics from random snapshots of heterogeneous ensembles

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There is mounting evidence that structural variability is common and important to function in biology , and that "structure" is neither static, nor immutable [1-6]. With the exception of NMR, however, current structure determination techniques must often assume the interrogated objects are identical. This includes crystallography, cryo-EM, and the recently burgeoning XFEL-based methods. The study of structural variability and dynamics thus represents an important, but difficult frontier in understanding biological processes. This talk will outline how a new generation of algorithms offers a powerful route to structure and dynamics through random interrogation of members of heterogeneous ensembles.

In collaboration with D. Giannakis, G.N. Phillips, Jr., P. Schwander, and C.H. Yoon.

[1] S.J. Ludtke, et al. *Structure* **2008**. *16*:441-448. [2] N. Fischer, et al. *Nature* **2010**. *466*:329-333. [3] S. H. W. Scheres, et al. *Nature Methods* **2007**. *4*:27-29. [4] J. Brink, et al. *Structure* **2004** *12*:185-191. [5] I. M. Yu, et al. *Science* **2008** 3*19*:1834-1837. [6] E. J. Levin, D. A. Kondrashov, G. E. Wesenberg, & G. N. Phillips, *Structure* **2007** *15*:1040-1052.

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MS.37.4

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Structure determination of biomolecules by XFEL radiation: exploitation of angular correlations of scattered intensities

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The more than billion-fold increase in the brightness over even synchrotron radiation offered by the x-ray free electron laser gives rise to the exciting possibility of biomolecular structure determination from illumination of individual molecules [1], or of small non-crystalline ensembles in solution or in a biomembrane. We will describe progress in developing novel theories for structure determination from this very new form of data.

One approach that has shown much promise is the extraction of structural information from angular correlations of scattered intensities [2,3]. Such an approach offers advantages of efficient compression of the voluminous data produced by high repetition-rate XFEL pulses, of dealing with very noisy data, and of the ability to extract information from disordered biomolecular ensembles closer to those found in nature.

We will describe the latest results of simulations of this appoach as well as some tests with experimental data [4]. We also discuss the possibility of exploiting another capability of ultrashort, ultrabright radiation pulses, namely that of determining rapid structural changes of biomolecules during the progress of a light-induced chemical reaction in a more natural environment, such as a solution or a biomembrane, in an experiment in which the molecules are excited by an optical pump beam and interrogated immediately afterwards by an x-ray beam, in anaology with time-resolved crystallography [5].